

chain nodes :

20 21

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

chain bonds :

19-20 20-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-8 6-19 7-8 7-12 7-19 8-9 9-10 10-11 11-12 12-15  
13-14 13-18 14-15 14-19 15-16 16-17 17-18

exact/norm bonds :

5-8 6-19 7-19 12-15 14-19 20-21

exact bonds :

19-20

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18 14-15  
15-16 16-17 17-18

isolated ring systems :

containing 1 : 7 : 13 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom  
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS  
21:CLASS

L9 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2002 ACS  
 AN 2002:276486 CAPLUS  
 DN 136:302731  
 TI DNA-based integrated circuit fabrication using dyes to change band gap  
 IN Chen, Boris  
 PA Taiwan  
 SO U.S. Pat. Appl. Publ., 11 pp.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002042151	A1	20020411	US 2001-964745	20010928
				TW 2000-89120427A	20001002

AB This Invention is a DNA-based integrated circuit fabrication using DNA dyeing technol. to change energy gap of the DNA mols. to alter the cond. of DNA mols. Because that the diam. of DNA mols. is only .apprx.2 nm, this kind of electronic element, which is not made with photolithog. technologies, not only avoids the bottleneck of line width in prodn. of photolithog.-based ICs, but also limits the line width to 2 nm, much less than the min. line width (0.13 .mu.m or 130 nm) in semiconductor prodn. industry. It brings a practical approach to IC design beyond photolithog. technologies, and ensures the development of ICs to levels predicted by the Moore Law.

L9 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2002 ACS  
 AN 2001:612321 CAPLUS  
 DN 136:48083  
 TI Transfer of 4'-chloro-2,2':6',2"-terpyridine platinum(II) between human serum albumin, glutathione and other thiolate ligands. A possible selective natural transport mechanism for the delivery of platinum(II) drugs to tumor cells  
 AU Ross, Steven A.; Carr, Carolyn A.; Briet, Jan-Willem; Lowe, Gordon  
 CS The Dyson Perrins Laboratory, Department of Chemistry, University of Oxford, Oxford, OX1 3QY, UK  
 SO Anti-Cancer Drug Design (2001), Volume Date 2000, 15(6), 431-439  
 CODEN: ACDDDEA; ISSN: 0266-9536

PB Oxford University Press  
 DT Journal  
 LA English

AB The antitrypanosomal and antitumor activities of (2,2':6',2"-terpyridine)platinum(II) complexes have been postulated to be due to their ability to inhibit irreversibly the NADPH/FAD redox enzymes trypanothione reductase and human thioredoxin reductase, resp. Here we show that these platinum(II) complexes metalate recombinant human albumin (rHA) at the single free thiol group (Cys-34). Moreover, the (2,2':6',2"-terpyridine)platinum(II) complex can be transferred from rHA to other thiols, such as 2-hydroxyethanethiol or glutathione. Human serum albumin could therefore provide a natural transport mechanism for the selective delivery of these agents to tumor cells by the enhanced permeability and retention (EPR) mechanism.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2002 ACS  
 AN 2001:581241 CAPLUS  
 DN 135:284878  
 TI Irreversible inhibitors of T. cruzi trypanothione reductase: Kinetic and crystallographic studies  
 AU Bonse, Susanne; Krauth-Siegel, R. Luise; Schlichting, Ilme; Lowe, Gordon  
 CS Center of Biochemistry, Heidelberg University, Germany  
 SO Flavins and Flavoproteins 1999, Proceedings of the International Symposium, 13th, Konstanz, Germany, Aug. 29-Sept. 4, 1999 (1999), 895-898.

Editor(s): Ghisla, Sandro. Publisher: Rudolf Weber, Agency for Scientific Publications, Berlin, Germany.

CODEN: 69BQDP

DT Conference

LA English

AB Trypanothione reductase (TR) is an FAD-disulfide oxidoreductase exclusively found in trypanosomatid parasites and recently - together with glutathione reductase (GR) - in *Euglena gracilis*. The enzyme which catalyzes the redn. of trypanothione disulfide (TS2) to trypanothione [T(SH)2, N1,N8-bis-(glutathionyl)spermidine]: TS2 + NADPH + H+ .fwdarw. T(SH)2 + NADP+ is a promising target for antitrypanosomal chemotherapy. Irreversibly binding compds. are attractive drug candidates since - in contrast to competitive inhibitors - accumulation of substrate due to the blockage of the pathway cannot overcome inhibition. In addn., covalent inhibitors may be applied in much lower concns. Known covalent inhibitors of TR are trivalent arsenicals and nitrosoureas which are not specific and very toxic also to the host. Here we report on the irreversible inhibition of *T. cruzi* trypanothione reductase by kukoamine A and newly designed platinum complexes.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2002 ACS

AN 2001:527782 CAPLUS

DN 135:251426

TI Human Thioredoxin Reductase Is Efficiently Inhibited by (2,2':6',2''-Terpyridine)platinum(II) Complexes. Possible Implications for a Novel Antitumor Strategy

AU Becker, Katja; Herold-Mende, Christel; Park, Jenny J.; Lowe, Gordon; Schirmer, R. Heiner

CS Interdisciplinary Research Center, Giessen University, Giessen, D-35392, Germany

SO Journal of Medicinal Chemistry (2001), 44(17), 2784-2792

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Malignant neoplasms of the brain represent the second leading cause of cancer-related mortality in children under the age of 15. The prognosis of patients with glioblastoma multiforme, the most malignant type of gliomas, remains poor offering a median survival time of only 1 yr. (2,2':6',2''-Terpyridine)platinum(II) complexes are known to possess DNA-intercalating activity and have been shown to be potential chemotherapeutic agents. In the present study we identified the selenoenzyme thioredoxin reductase (TrxR) as a major target of (2,2':6',2''-terpyridine)platinum(II) complexes. New complexes were synthesized to optimize this inhibition. The NADPH-reduced enzyme is inhibited almost stoichiometrically by the complexes involving a reversible competitive and an irreversible tight-binding component. For the most potent inhibitor, N,S-bis(2,2':6',2''-terpyridine)platinum(II)-thioacetimine trinitrate, the Ki for the competitive component of the inhibition is 4 nM and the IC50 for the tight-binding component is 2 nM after an incubation time of 5 min. The closely related but non-selenium-contg. enzyme glutathione reductase is much less inhibited (by a factor of >1000). The platinum complexes were found to strongly inhibit the proliferation of three different glioblastoma cell lines as well as of two different head-and-neck squamous carcinoma cell lines. In a glioblastoma cell culture, less than 10 .mu.M of a platinum(II) compd. caused an initial drop of hTrxR activity which was followed by an increase of activity in the surviving cells. A 10 .mu.M inhibitor added every 24 h led to 4% residual hTrxR activity but 100% glutathione reductase activity in the cells surviving for 67 h. The potential of (2,2':6',2''-terpyridine)platinum(II) complexes acting simultaneously at two different intracellular targets-hTrxR and DNA-as antitumor agents is discussed.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:45514 CAPLUS  
DN 134:346330  
TI Exciplex quenching of photoexcited platinum(II) terpyridines: influence of the orbital parentage  
AU Crites Tears, D. K.; McMillin, D. R.  
CS Department of Chemistry, Purdue University, West Lafayette, IN, 47907-1393, USA  
SO Coordination Chemistry Reviews (2001), 211, 195-205  
CODEN: CCHRAM; ISSN: 0010-8545  
PB Elsevier Science S.A.  
DT Journal; General Review  
LA English  
AB Quenching studies involving a range of Lewis bases established that exciplex quenching can affect the lifetime of the emissive charge-transfer state of a platinum(II) terpyridine. The evidence comes from studies of Pt(trpy)SCN<sup>+</sup>, where trpy denotes 2,2':6',2''-terpyridine, and a Pt(4'-X-T)Cl<sup>+</sup> series where 4'-X-T denotes a 4'-substituted trpy deriv. and X is a CN, SMe or NMe<sub>2</sub> substituent. Thus, in dichloromethane the quenching rate const. increased with the donor no. as the quencher varied from a relatively weak base like acetonitrile or acetone to a stronger donor like DMSO or pyridine. For the thiocyanate complex in particular, the quenching rate increased by almost three orders of magnitude. Within the Pt(4'-X-T)Cl<sup>+</sup> series, the rates showed a marked variation with the electron-donating ability of the substituent X. Thus, with pyridine as the quencher, the rate const. varied from 3.5.times.10<sup>8</sup> to 1.0.times.10<sup>10</sup> M<sup>-1</sup>s<sup>-1</sup> as X changes from NMe<sub>2</sub> to CN. Variations in the orbital parentage of the excited state account for the trend because the Lewis acidity of the metal center decreased with the delocalization of the hole onto the ligand. When the rate of exciplex formation was slow, an outer-sphere complex accumulated in soln. and the kinetic plots show satn. behavior at high quencher concns. A review with 37 refs.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:820326 CAPLUS  
DN 134:144401  
TI (2,2':6',2''-Terpyridine)platinum(II) Complexes Are Irreversible Inhibitors of Trypanosoma cruzi Trypanothione Reductase But Not of Human Glutathione Reductase  
AU Bonse, Susanne; Richards, Jonathan M.; Ross, Steven A.; Lowe, Gordon; Krauth-Siegel, R. Luise  
CS Biochemie-Zentrum Heidelberg, Heidelberg University, Heidelberg, D-69120, Germany  
SO Journal of Medicinal Chemistry (2000), 43(25), 4812-4821  
CODEN: JMCMAR; ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
AB (2,2':6',2''-Terpyridine)platinum(II) complexes possess pronounced cytostatic activities against trypanosomes and leishmania. As shown here, the complexes are irreversible inhibitors of trypanothione reductase (TR) from Trypanosoma cruzi, the causative agent of Chagas' disease. The most effective derivs. are the (4'-chloro-2,2':6',2''-terpyridine)platinum(II) ammine and the (4'-picoline)(4'-p-bromophenyl-2,2':6',2''-terpyridine)platinum(II) complexes which in the presence of NADPH inhibit TR with second-order rate consts. of about 1.3.times.10<sup>4</sup> M<sup>-1</sup>s<sup>-1</sup>. The modified enzyme species possess increased oxidase activities. The inhibition is not reversed upon dialysis or treatment with low-mol.-mass thiols. Kinetic and spectroscopic data suggest that Cys52 in the active

site has been specifically altered. Inhibition of this key enzyme of parasite thiol metab. probably contributes to the antitrypanosomal activity of the compds. In contrast to the parasite enzyme, most (terpyridine)platinum complexes interact only reversibly with human glutathione reductase and an initial inhibition is completely abolished during the course of the assay.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:635540 CAPLUS  
DN 133:368727  
TI Synthetic Incorporation of Metal Complexes into Nucleic Acids and Peptides  
Directed toward Functionalized Molecules  
AU Shionoya, Mitsuhiko; Tanaka, Kentaro  
CS Dep. Chem., Grad. Sch. Sci., The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan  
SO Bulletin of the Chemical Society of Japan (2000), 73(9), 1945-1954  
CODEN: BCSJA8; ISSN: 0009-2673  
PB Chemical Society of Japan  
DT Journal  
LA English  
OS CASREACT 133:368727  
AB Novel synthetic approaches for incorporation of metal complexes into nucleic acids and peptides are described. First, novel artificial .beta.-C-nucleosides bearing a chelator nucleobase (2-aminophenol, catechol, or o-phenylenediamine) were synthesized. These artificial nucleobases were introduced for alternative base pairing through metal coordination instead of the hydrogen bonding in natural DNA. 1H NMR and mass spectral studies clearly showed that o-phenylenediamine-type nucleoside forms a stable 2:1 square-planar complex with a PdII ion, providing an alternative DNA base pairing through metal complexation. Secondly, an efficient strategy for the liq.-phase synthesis of cyclic metalloptides having a repeating Gly-L-Cys(terpyPtII) sequence, cyclo[-Gly-L-Cys(terpyPtII)-]nCln (n = 3, 4), was developed. These cyclic metalloptides were obtained by cyclization of the corresponding linear peptides, H2[-Gly-l-Cys(terpyPtII)-]nOH.cntdot.(CF3CO2)n+1 (n = 3, 4), in moderate yields. The former cyclic hexapeptide was found to act as a pos. charged anion receptor. This synthetic approach would provide a powerful tool for arraying metal centers on cyclopeptide frameworks.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2002 ACS  
AN 2000:608755 CAPLUS  
DN 133:202250  
TI Preparation and antiprotozoal, anti-rheumatoid arthritis and antitumor activities of platinum(II) terpyridine thiolate compounds  
IN Lowe, Gordon  
PA Isis Innovation Limited, UK  
SO PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DT Patent  
LA English

FAN.CNT 1

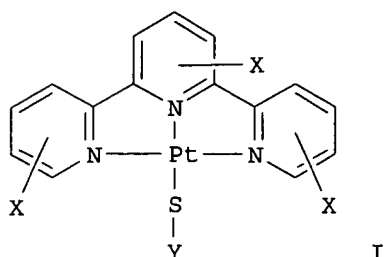
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050431	A1	20000831	WO 2000-GB686	20000225
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1155025 A1 20011121 GB 1999-4523 A 19990226  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO EP 2000-906490 20000225

GB 1999-4523 A 19990226  
WO 2000-GB686 W 20000225

OS MARPAT 133:202250  
GI



AB The prepn. is described of platinum(II) complexes (I) wherein each X, which may be the same or different, is hydrogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, aralkyl, alkaryl, acyl, halogen, haloalkyl, haloaryl, hydroxyalkyl, hydroxyaryl, aminoalkyl, aminoaryl, primary, secondary or tertiary amine, hydrazine, alkylhydrazine, alkoxyl, alkylthio, aralkoxyl, nitrile, ester, amide, nitro, azide or aziridino, or is a covalently linked chain which is joined to at least one other complex (I) so as to form a dimeric or oligomeric species, or a covalently linked moiety which provides recognition for a target receptor; and Y is alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aralkyl, heterocyclyl, an inorg. oxyacid or inorg. oxyacid deriv., or a covalently linked chain which is joined to at least one other complex (I) so as to form a dimeric or oligomeric species; or a pharmaceutically acceptable salt thereof, for use in a method of treatment of the human or animal body by therapy. In particular, the compds. are for use as antiprotozoal, anti-rheumatoid arthritis or antitumor agents. Thus, 2-hydroxyethanethiolato(2,2':6',2''-terpyridine)platinum(II) nitrate was prepd. and its antiprotozoal and antitumor activities were measured.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2002 ACS

AN 1999:774703 CAPLUS

DN 132:174885

TI Cyclic metallopeptides, cyclo[Gly-L-Cys(terpyPtII)]nCl<sub>n</sub>

AU Tanaka, Kentaro; Shionoya, Mitsuhiko; Shigemori, Kazuki

CS Coordination Chemistry Laboratories, Institute for Molecular Science,  
Okazaki, 444-8585, Japan

SO Chemical Communications (Cambridge) (1999), (24), 2475-2476

CODEN: CHCOFS; ISSN: 1359-7345

PB Royal Society of Chemistry

DT Journal

LA English

AB An efficient strategy for the liq.-phase synthesis of cyclic metallopeptides, cyclo[Gly-L-Cys(terpyPtII)]nCl<sub>n</sub> (n = 3, 4), was developed, which could provide a powerful tool for arraying metal centers on cyclopeptide frameworks. The synthetic method involves complexation of the linear peptide H<sub>2</sub>(Gly-L-Cys)nOH.(CF<sub>3</sub>CO<sub>2</sub>) with [(terpy)PtCl]Cl in aq. soln. at room temp. to give the S-coordinated (protected) chain peptides

$H_2[Gly-L-Cys(terpyPtII)]_nOH.(CF_3CO_2)_{n+1}$ , which are cyclized in  $H_2O-MeCN$  at 25.degree. in the presence of HOBt and EDC. The protecting (and cyclization-promoting) (terpy)Pt moieties are readily removed by treatment with TFA to afford the corresponding cyclopeptide. The cyclic metallopeptides act as pos. charged anion receptors; the cyclohexapeptide deriv. selectively sepd. benzene-1,3,5-tricarboxylate anion from an equimol. mixt. of the 1,2,3-, 1,2,4- and 1,3,5-tricarboxylates.